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Supplemental Information

Adipocyte Reprogramming by the Transcriptional Coregulator GPS2 Impacts Beta Cell Insulin Secretion

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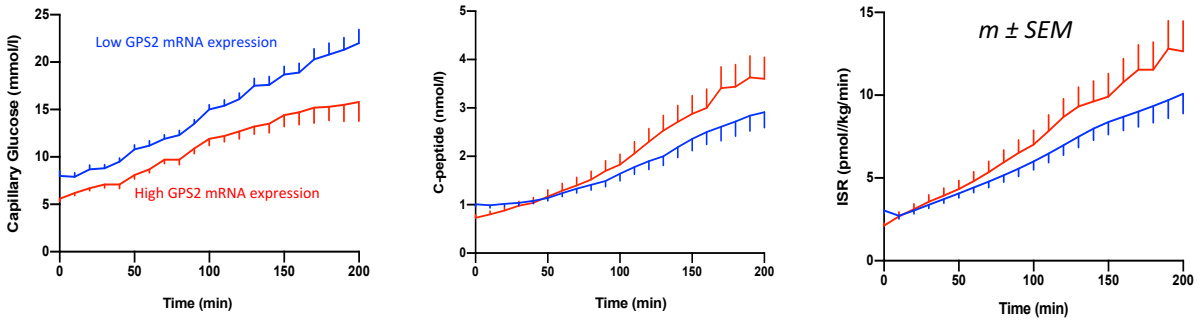
	Low GPS2 mRNA expression	High GPS2 mRNA expression	*p*
N	12	11	
GPS2 mRNA expression*	0.30 [0.32]	0.98 [0.51]	*<0.0001*
Sex: men (%)	75	60	*0.65*
Age (y)	48 ± 13	48 ± 10	*0.96*
BMI (kg/m^2)	29.1 ± 2.7	30.8 ± 4.0	*0.24*
T2DM: N (%)	10 (92)	4 (40)	*0.02*
HbA1c (%)	7.0 ± 0.5	5.8 ± 0.3	*<0.0001*
SBP (mmHg)	126 ± 14	122 ± 15	*0.52*
DBP (mmHg)	82 ± 10	78 ± 10	*0.30*
Total cholesterol (mmol/l)	4.65 ± 0.96	4.99 ± 1.40	*0.49*
Triglycerides (mmol/l)	1.16 ± 0.21	1.25 ± 0.86	*0.79*
Creatinine (µmol/l)	82 ± 17	73 ± 19	*0.27*

Supplementary Table S1 (Related to Figure 1): Clinical and anthropometric human data.
Mean ± SD or *median [IQR]

A



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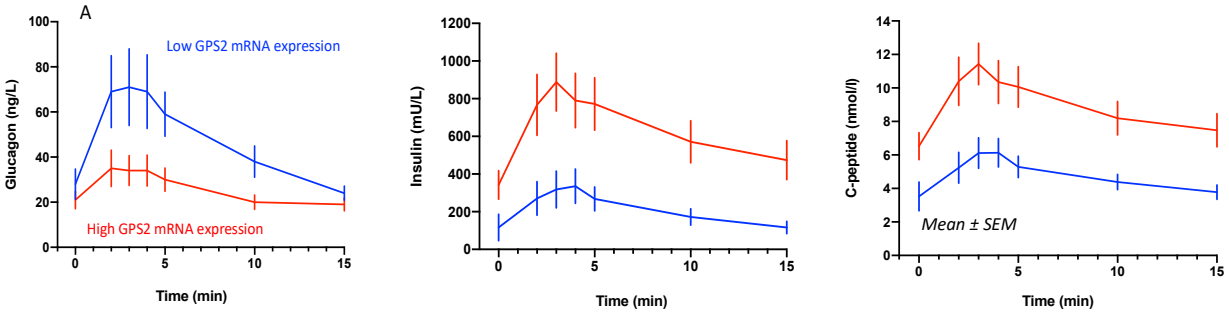

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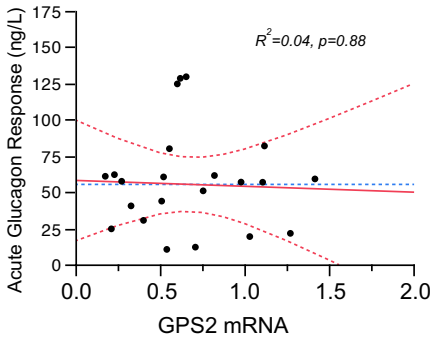
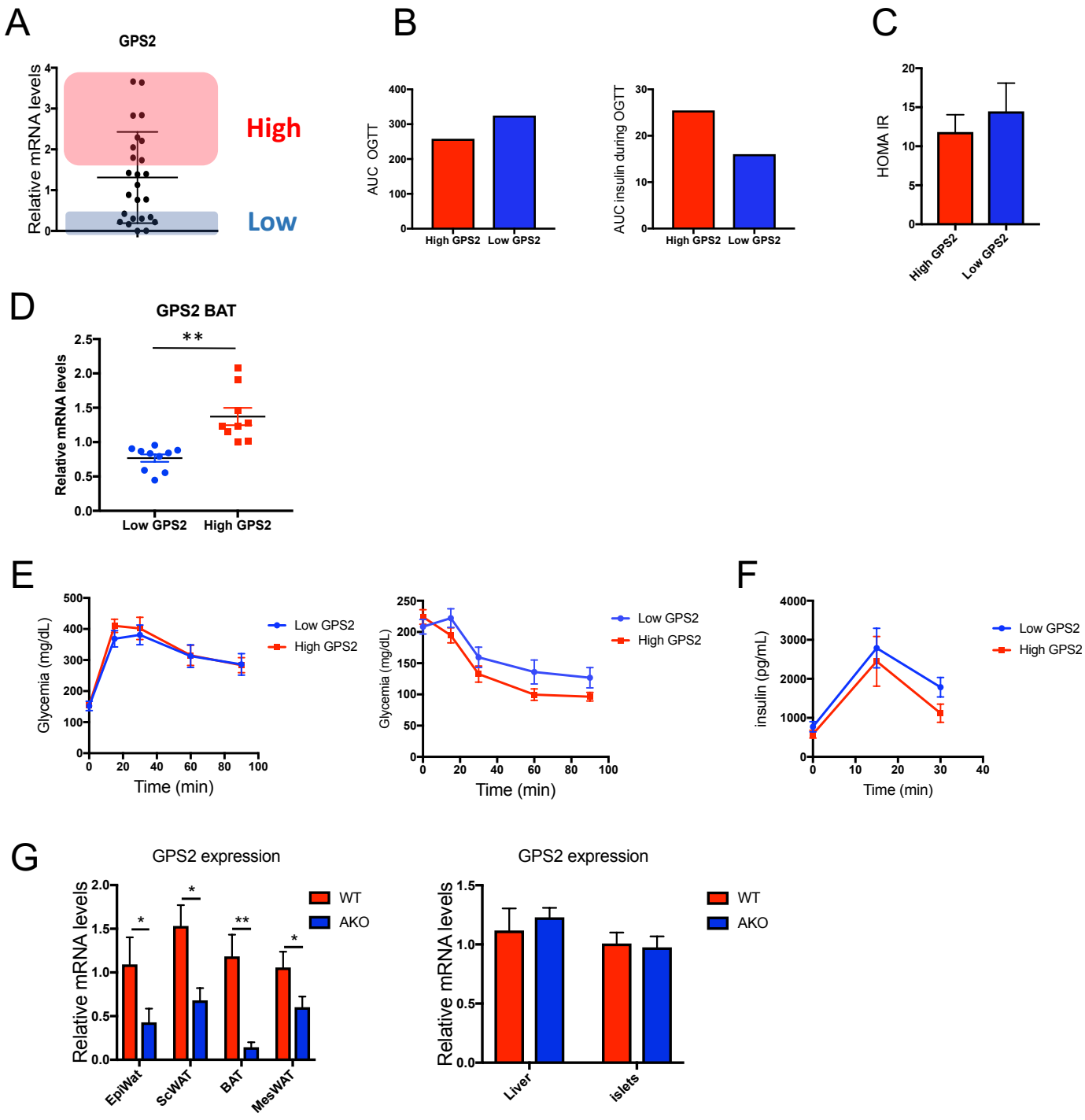
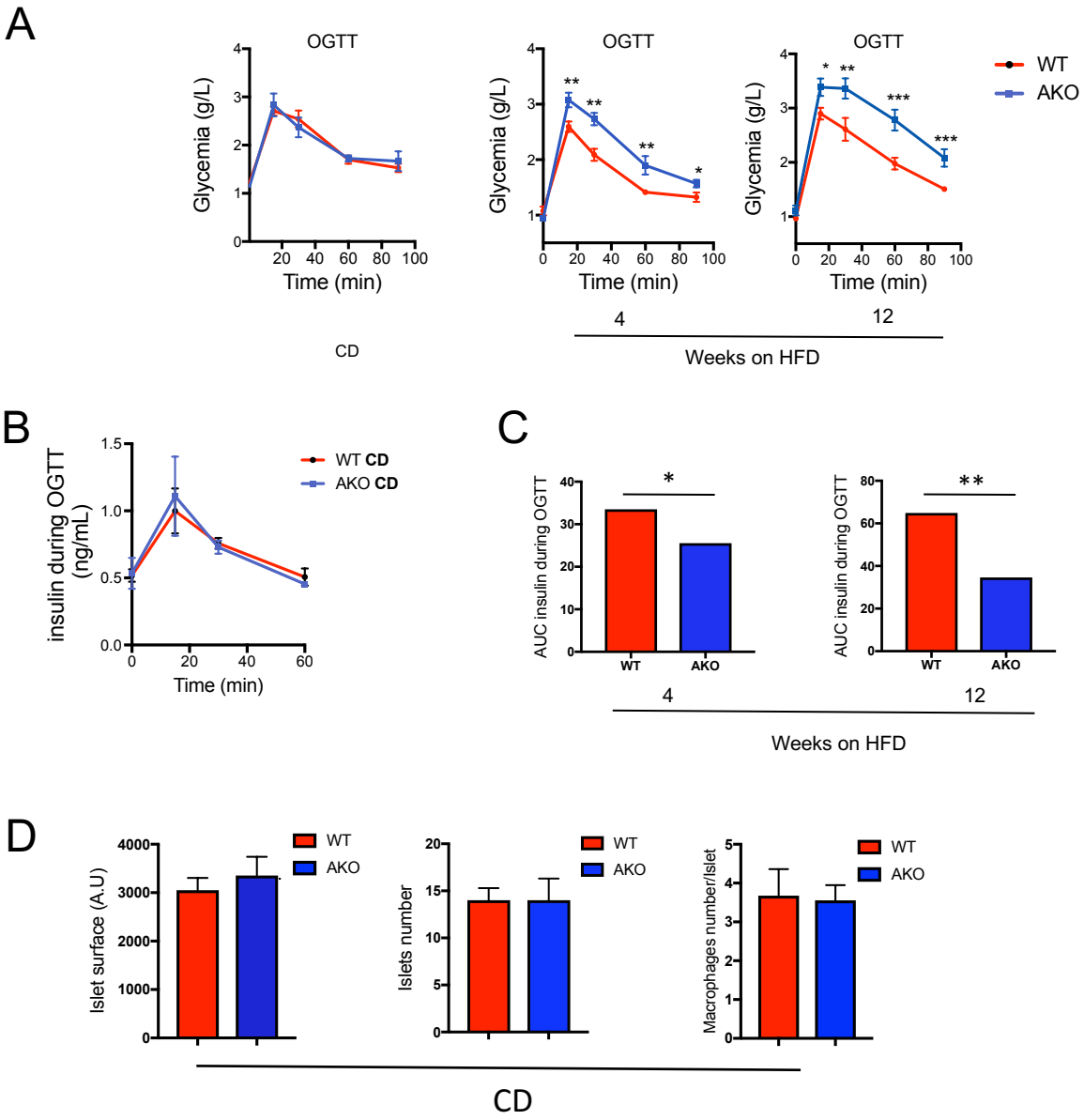


*adjusted for sex, age, glycemic status (T2DM or ND), and pre-arginine injection glucose and insulin levels

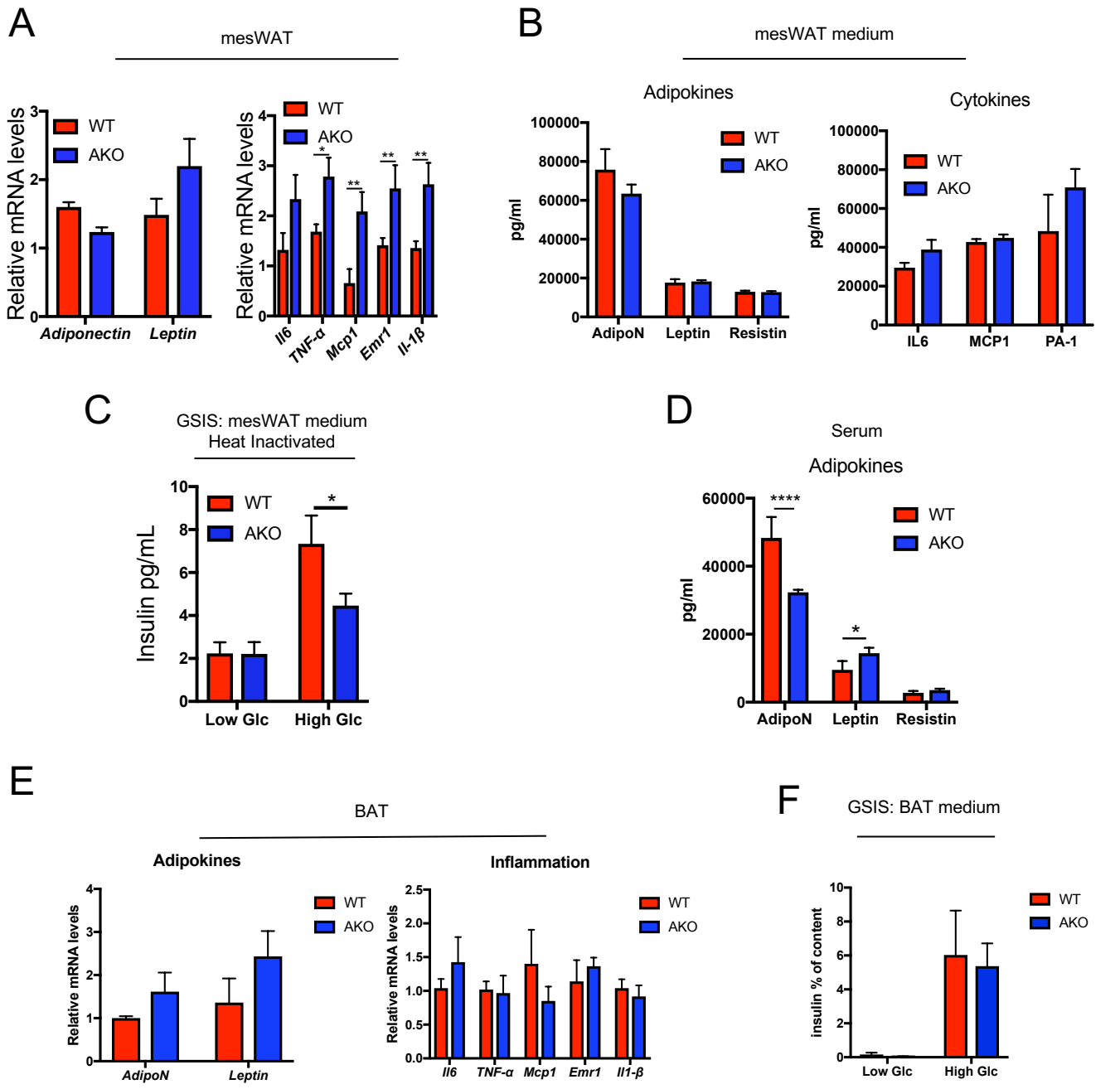
Supplementary Figure S1 (Related to Figure 1): (A) Capillary blood glucose, plasma C-peptide and Insulin Secretion Rate (ISR) during a graded glucose infusion. Participants were stratified by GPS2 mRNA expression as Low or High expression as per values below (n=12) or above the median (n=11), respectively. (B) Glucagon, Insulin and C-peptide levels during a glucose-dependent arginine stimulation by adipocyte GPS2 mRNA expression. (C) Correlation of Acute Insulin Response (AIR) during a glucose-dependent arginine stimulation and adipocyte GPS2 mRNA expression in multivariate analyses. Correlation adjusted for sex, age, glycemic status (T2DM or ND), and pre-arginine injection glucose levels



Supplementary Figure S2 (Related to Figure 2) : (A) RT-qPCR analysis of *GPS2* in eWAT from WT C57BL6/J under High Fat Diet (HFD) during 12 weeks (n= 28). (B) Area Under the Curve (AUC) of the OGTT of figure 2B and 2C. (C) Index of Insulin resistance (HOMA-IR) of GPS2 low versus high expression in WAT of high fat fed mice for 12 weeks (n=9 in each group). (D) RT-qPCR analysis of *GPS2* in BAT from WT C57BL6/J under High Fat Diet (HFD) during 12 weeks (n=19). (E). Oral Glucose Tolerance Test (OGTT) and insulin tolerance test (ITT) in WT C57BL6/J after 12 weeks of HFD classified into 2 groups: high GPS2 expression (n=9) and low GPS2 expression (n=10). (F) Measurements of insulin secretion during the Oral Glucose Tolerance Test in WT C57BL6/J after 12 weeks of HFD classified into 2 groups: high GPS2 expression (n=9) and low GPS2 expression (n=9). (G) RT-qPCR analysis of *GPS2* in eWAT , scWAT, mesWAT, BAT, liver and islets from WT and GPS AKO mice on CD (n= 5-6). All data are represented as mean ± S.E.M. *P <0.05, ** P <0.01, *** P <0.001.



Supplementary Figure S3 (Related to Figure 2 and 3) : (A) Oral Glucose Tolerance Test (OGTT) in WT controls and GPS2 AKO after CD ,4 and 12 weeks of HFD (CD=4-5, 4 weeks HFD n=6, 12 weeks HFD n= 5-6). (B) Insulin concentration measured during OGTT in in WT controls and GPS2 AKO C57BL6 after CD (n=4-5). (C) Area Under the Curve (AUC) of insulin concentration during the OGTT of figure 2F. All data are represented as mean ± S.E.M. *P <0.05, ** P <0.01, *** P <0.001. (D) Measurements of islets surface and number and macrophages number in pancreas from WT and GPS2 AKO mice under CD (n=4-5). All data are represented as mean ± S.E.M. *P <0.05, ** P <0.01, *** P <0.001.



Supplementary Figure S4 (related to Figure 4): (A and B) WAT Gene expression and WAT secretome analysis of mesWAT from WT and GPS2 AKO mice after 12 weeks of HFD (n=4). (C) Glucose Stimulated Insulin Secretion (GSIS) of islets from WT C57BL6/J mice cultured with mesWAT heat inactivated culture medium for 12h and treated for 2 h with low (2.8 mM) or high (16,7 Mm) glucose. Results are expressed in % of insulin content (n=3). (D) Serum concentration of adiponectin (AdipoN), leptin and resistin of WT and GPS2 AKO mice after 12 weeks of HFD (n=6 in each group). (E) Measurement of adipokines and inflammatory genes by RT-qPCR in BAT from WT and GPS2 AKO mice in 12 weeks of HFD (n=5-6). (F) Glucose Stimulated Insulin Secretion (GSIS) of islets from WT C57BL6/J mice cultured with BAT culture medium for 12h and treated for 2 H with low glucose (Low Glc) (2.8 mM) and high glucose (High Glc) (16,7 Mm). All data are represented as mean ± S.E.M. *P <0.05, ** P <0.01, *** P <0.001.